

Applicants : Carolyn E. Mountford et al.  
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D. Remarks

Reconsideration and allowance in view of the amendments made and comments which follow are respectfully requested.

Claims 1-26 were pending in this application. Claims 1, 9, 15, 19, 23, 24, 25 and 26 are being amended. Claims 1-26 are now pending.

In the Office Action, claims 1-26 were rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over MacKinnon (Radiology, 1997) in view of Somorjai (Magnetic Resonance in Medicine, 1995). The Examiner stated that in the paper MacKinnon discusses fine-needle biopsy specimens of benign breast lesions distinguished from invasive cancer ex vivo with proton MR spectroscopy to determine whether invasive breast cancer can be distinguished from benign lesions with proton magnetic resonance (MR) spectroscopy ex vivo on the basis of altered cellular chemistry. The Examiner stated that the MacKinnon paper concluded that proton MR spectroscopy of fine-needle biopsy specimens provides objective diagnostic information that complements findings of conventional preoperative investigations of breast lesions. The Examiner stated that relative to the instant claims is the paragraph bridging the column 2-3 of page 664. The Examiner stated that the last sentence of the paragraph cites the Somorjai reference and teaches that the multivariate techniques of the reference are "likely to improve sensitivity and specificity" of the analysis.

The Examiner stated that in the paper Somorjai presents computerized consensus diagnosis as a classification strategy for the robust analysis of <sup>1</sup>H MR spectra of thyroid neoplasms. The

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Examiner stated that they developed and applied a new classification strategy called computerized consensus diagnosis (CCD) to provide robust, reliable classification of biomedical data. The Examiner stated that the strategy involves the cross-validated training of several classifier of diverse conceptual and methodological origin on the same data, and appropriately combining their outcomes. The Examiner stated that the paragraph that bridges pages 258-259 the formation of training and testing sets from the data is explained, wherein the training set was cross validated by the leave-one out (LOO) method in which one fewer than the total number of samples are included in the training set, classifying the excluded sample and repeating the procedure until each sample has been excluded from the reduced training set. The test set is then classified with an optimal classifier that was retrained on all of the samples in the training set. The strategy is tested on proton magnetic resonance spectra of human thyroid biopsies, which are successfully allocated to normal or carcinoma classes. Linear Discriminant Analysis was used as independent classifiers on two spectral regions, and the median of the six classification outcomes was chosen as the consensus. The Examiner stated that the use of the leave-one out method in the Linear Discriminant Analysis is taught on page 259 on the last paragraph of the left column, and the paragraph bridging pages 260-261 teaches the formation of multiple training sets along with the reasons therefore. The Examiner stated that the paragraph bridging pages 261-262 teaches that because of this cross validation method each individual sample in the test set has a probability assigned relative to the class that it belongs. The Examiner stated that this procedure yielded 100% specificity and 100% sensitivity on the training sets, and 100% specificity and 98% sensitivity on samples of known malignancy in the test sets. The Examiner stated that they discuss the

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necessary steps any classification approach must take to guarantee reliability, and stress the importance of fuzziness and undecidability in robust classification. The Examiner stated that the last page presents further refinements that would reduce some of the problems or improve some of the results.

The Examiner stated that it would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the multivariate analysis methodology of Somorjai into the MacKinnon analysis of breast tissues because of the statement by MacKinnon directing one of the Somorjai multivariate method as likely to provide improved results and the teaching of improved analysis results by Somorjai.

In rebutting applicant's arguments filed June 13, 2003 the Examiner stated that the argument that the Somorjai reference does not teach repeating the cross validation step or the weighted average can best be answered by looking at the reference. The Examiner stated that in the paragraph that bridges pages 258-259 the formation of training and testing sets from the data is explained. The Examiner stated that the training set was cross validated by the leave-one-out method in which one fewer than the total number of samples are included in the training set, classifying the excluded sample and repeating the procedure until each sample has been excluded from the reduced training set. The Examiner stated that the test set is then classified with an optimal classifier that was retrained on all of the samples in the training set. The Examiner stated that paragraph bridging pages 260-261 teaches the formation of multiple training sets along with the reasons therefore. Thus, the Examiner stated, the cross validation procedure is performed a number of times for each training set. The Examiner stated that the

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paragraph bridging pages 261-262 teaches that because of this cross validation method each individual sample in the test set has a probability assigned relative to the class that it belongs. The Examiner stated that this would indicate some sort of a weighted average for the formation of the optimal classifier that is used on the test set of samples.

The Somorjai reference cited by the Examiner reports on earlier work of co-inventors herein, and applicants are familiar with this work.

The Somorjai reference does not disclose clause (b) of claim 1 which recites that in the cross-validation step, a first portion of the spectra selected, wherein the first portion is about one-half of the total spectra. In the Somorjai reference, a leave-one out (LOO) process is employed, wherein only one of the spectra is left out and the remainder is all the spectra less one. Nowhere does Somorjai disclose having a training set and a test set each having about one-half of the total spectra.

Even if the MacKinnon and Somorjai references were combined as proposed by the Examiner, claim 1 is patentable at least because Somorjai fails to disclose the features discussed above.

In view of the foregoing, applicant urges that independent claims 1, 9, 15, 19, 23, 24, 25 and 26 are patentable over the prior art cited, for at least for the same reasons given above in connection with claim 1.

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If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invites the Examiner to telephone them at the number provided below.

No additional fee is deemed necessary in connection with the filing of this Response. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

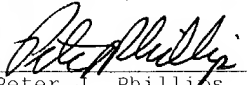
Respectfully submitted,



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